

Complex noise in diffusion-limited reactions of replicating and competing species

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(Dated: February 6, 2008)

We derive exact Langevin-type equations governing quasispecies dynamics. The inherent multiplicative noise has both real and imaginary parts. The numerical simulation of the underlying *complex* stochastic partial differential equations is carried out employing the Cholesky decomposition for the noise covariance matrix. This noise produces unavoidable spatio-temporal density fluctuations about the mean field value. In two dimensions, the fluctuations are suppressed only when the diffusion time scale is much smaller than the amplification time scale for the master species.

PACS numbers: 05.10.Gg, 05.40.Ca, 05.10.-a, 82.40.Ck

I. INTRODUCTION

Deterministic descriptions of reacting and diffusing chemical and molecular species fail to account for the system's internal fluctuations. Nevertheless, it is known that if the spatial dimensionality d of the system is smaller than a certain upper critical dimension d_c , these intrinsic fluctuations can play a crucial role in the asymptotic late time behavior of decay rates (anomalous kinetics) and the results obtained from the mean field equations are not correct [1]. Even far from the asymptotic regimes, these fluctuations can also control the dynamics on local spatial and temporal scales [2]. The mean field result is only valid in the idealized infinite diffusion limit, because the reactions themselves induce local microscopic density fluctuations that must be taken into account in the underlying nonlinear dynamics.

The proper inclusion of the effects of microscopic density fluctuations in reaction-diffusion systems can be carried out once the microscopic kinetic equations are specified. With the reaction scheme in hand, one can derive the corresponding continuous-time master equation, then represent this stochastic process by second-quantized bosonic operators and in the final step, pass to a path integral to map the system onto a continuum stochastic field theory [3, 4]. This technique has opened up the way for employing powerful field-theoretic renormalization group (RG) methods for studying fluctuations in a number of simple reaction-diffusion problems [5]. Moreover, effective Langevin-type equations can be deduced from these field-theoretic actions, in which the noise is made manifest and is specified precisely. Langevin-type equations are ideally suited for investigating problems in stability and pattern formation, and lend themselves for the direct numerical solution of the dynamics. However, most of the studies devoted to fluctuations in reaction-diffusion systems are based on applying RG methods to the field-theoretic actions, with little attention being payed to the analytical or numerical study of the associated effective Langevin equations. This is most likely due to the fact that the noise in this latter representation is often imaginary or even complex, a feature, which at first glance, may be somewhat surprising [6], and has presented a challenging problem for numerical simulation.

The purpose of this paper is to confront this imaginary/complex noise issue at face value. We propose and test out an algorithm for numerically integrating complex noise in multi-component reaction-diffusion equations [7]. The model we treat can be considered as a single quasispecies with error tail, which is analytically and computationally amenable. The current great revival of interest in quasispecies dynamics owes to the fact that viral population dynamics is known to be described by quasispecies [8]. The major part of this work has been devoted to the analysis of their dynamics under spatially homogeneous conditions [8, 9, 10, 11, 12]. More recently, the importance of diffusive forces has been recognized and taken into account [13, 14], but rather less attention has been payed to the presence of the unavoidable internal density fluctuations [15] that are necessarily present in all realistic incompletely mixed diffusing systems of reacting agents [16]. In view of the above considerations, it is important to understand how internal fluctuations affect the evolution of replicator dynamics, and in what ways do the deterministic and stochastic effects compete. The specific model treated here maps exactly to a set of Langevin equations. The advantage for

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the numerical simulation is that the model has few fields, the corresponding noise terms are known exactly, and no approximation is required.

In Section II we introduce the specific reaction scheme. Following a well-established procedure [5], we derive a field theoretic description of these reactions by means of the Doi-Peliti formalism [3, 4]. We obtain the continuum action, and from this derive an equivalent and exact Langevin equation description of this quasispecies model. The advantage of this is that the noise properties are specified automatically and indicate how the naive mean field reaction-diffusion equations must be modified to take into account properly the (unavoidable) internal density fluctuations. The ensuing noise is *complex* and multiplicative, and in magnitude is controlled by the competition between the replicator amplification and diffusion. Their numerical solution is rendered possible by employing the Cholesky decomposition for the associated noise covariance matrix, as we describe in detail below in Section III. In Sec IV we present results of the numerical simulations of the complex Langevin equations derived in Sec III. Conclusions are drawn in Sec V.

II. FROM THE REACTION SCHEME TO THE STOCHASTIC PDES

A. The Model

We consider a simple replicator model with error introduced via the faulty self-replication into a mutant species. The mutant species or, error-tail, undergoes non-catalyzed self-reproduction, but has no effect on the main species. The system is closed, only energy can be exchanged with the surroundings, where activated monomers react to build up self-replicative units. These energy rich monomers are regenerated from the by-product of the reactions by means of a recycle mechanism (driven by an external source of photons–sunlight) maintaining the system out of equilibrium. The closure of the system directly imposes a selection pressure on the population. In what follows, M^* , I , I_e denote the concentrations of the activated energy rich monomers, the replicators and the mutant copies, respectively. The kinetic constants are introduced in the reaction steps as follows:

Accurate noncatalytic replication with rate A :



Error noncatalytic replication:



Error-species replication with rate A_e :



Species degradation and subsequent monomer reactivation with rates r, r_e :



The quality factor $Q \in [0, 1]$. In order to keep the following development mathematically manageable, we will assume that the monomer reactivation step proceeds sufficiently rapidly so that we can in effect, regard the decay of I and I_e plus the subsequent reactivation $M \xrightarrow{\text{energy}} M^*$ as occurring in *one* single step as indicated in Eq.(4,5). If we suppose the system is being bathed continuously by an external energy source, the monomer reactivation is occurring continuously, and this should be a reasonable approximation. To complete the specification of the model, we will include spatial diffusion. We allow the M^* , I and I_e particles to diffuse with constants D_s , D_I and D_e , respectively. Diffusion is incorporated at the outset in the master equation. The constraint of constant total particle number is *automatically* satisfied by the continuous chemical fields in the mean-field limit, as we demonstrate below. Most importantly, this constraint provides a selection pressure on the quasispecies. In the following, we keep the dependence on the model parameters general, though later on we will choose $D_s \gg D_I = D_e$ and $r = r_e$.

B. Mapping to bosonic field theory

This chemical master equation for the model Eqs.(1,2,3,4,5) can be mapped to a second-quantized description following a procedure developed by Doi [3]. Briefly, we introduce annihilation and creation operators a and a^\dagger for M^* , b and b^\dagger for I and c and c^\dagger for I_e at each lattice site, with the commutation relations $[a_i, a_j^\dagger] = \delta_{ij}$, $[b_i, b_j^\dagger] = \delta_{ij}$ and $[c_i, c_j^\dagger] = \delta_{ij}$. The vacuum state (corresponding to the configuration containing zero particles) satisfies $a_i|0\rangle = b_i|0\rangle = c_i|0\rangle = 0$. We then define the time-dependent state vector

$$|\Psi(t)\rangle = \sum_{\{k\}, \{m\}, \{n\}} P(\{k\}, \{m\}, \{n\}, t) \prod_i (a_i^\dagger)^{k_i} (b_i^\dagger)^{m_i} (c_i^\dagger)^{n_i} |0\rangle, \quad (6)$$

where $P(\{k\}, \{m\}, \{n\}, t)$ is the probability distribution to find k, m, n particles of type M^* , I , I_e , respectively, at each site. The master equation can then be written as a Schrödinger-like equation

$$-\frac{\partial |\Psi(t)\rangle}{\partial t} = H |\Psi(t)\rangle, \quad (7)$$

where the lattice hamiltonian or time-evolution operator is a function of $a, a^\dagger, b, b^\dagger, c, c^\dagger$ and is given by

$$\begin{aligned} H = & \frac{D_s}{l^2} \sum_{(i,j)} (a_i^\dagger - a_j^\dagger)(a_i - a_j) + \frac{D_I}{l^2} \sum_{(i,j)} (b_i^\dagger - b_j^\dagger)(b_i - b_j) + \frac{D_e}{l^2} \sum_{(i,j)} (c_i^\dagger - c_j^\dagger)(c_i - c_j) \\ & - A Q \sum_i \left[a_i b_i^\dagger b_i^\dagger b_i - a_i^\dagger a_i b_i^\dagger b_i \right] - A(1-Q) \sum_i \left[a_i b_i^\dagger b_i c_i^\dagger - a_i^\dagger a_i b_i^\dagger b_i \right] \\ & - A_e \sum_i \left[a_i c_i^\dagger c_i^\dagger c_i - a_i^\dagger a_i c_i^\dagger c_i \right] - r \sum_i \left[a_i^\dagger b_i - b_i^\dagger b_i \right] - r_e \sum_i \left[a_i^\dagger c_i - c_i^\dagger c_i \right]. \end{aligned} \quad (8)$$

Now take the continuum limit ($l \rightarrow 0$), and obtain a representation as a path integral [4] over continuous fields $a(x, t), a^*(x, t), b(x, t), b^*(x, t), c(x, t)$ and $c^*(x, t)$ with a weight $\exp(-S[a, a^*, b, b^*, c, c^*])$, whose action S is given by

$$\begin{aligned} S = & \int dt d^d x \left[a^* \partial_t a + D_s \nabla a^* \nabla a + b^* \partial_t b + D_I \nabla b^* \nabla b + c^* \partial_t c + D_e \nabla c^* \nabla c - A Q (ab^{*2} b - a^* a b^* b) \right. \\ & \left. - A(1-Q) (ab^* b c^* - a^* a b^* b) - A_e (ac^{*2} c - a^* a c^* c) - r(a^* b - b^* b) - r_e (a^* c - c^* c) \right]. \end{aligned} \quad (9)$$

The stationarity conditions (the ‘‘classical field equations’’) $\delta S/\delta a = \delta S/\delta b = \delta S/\delta c = 0$ and $\delta S/\delta a^* = \delta S/\delta b^* = \delta S/\delta c^* = 0$ yield, respectively, $a^* = b^* = c^* = 1$ and the usual *mean-field* rate equations

$$\partial_t a = D_s \nabla^2 a - A a b - A_e a c + r b + r_e c \quad (10)$$

$$\partial_t b = D_I \nabla^2 b + A Q a b - r b \quad (11)$$

$$\partial_t c = D_e \nabla^2 c + A(1-Q) a b + A_e a c - r_e c. \quad (12)$$

We emphasize that these equations represent the mean field approximation wherein all fluctuations are simply ignored. The *exact* and correct dynamical equations are fully stochastic, and we derive them below. Note in the mean field limit, the total particle number N is automatically conserved: adding up Eq. (10,11,12) allows us to prove that for a closed reaction system (in a bounded and closed reaction domain)

$$\frac{dN}{dt} = \frac{d}{dt} \int d^d x (a(x, t) + b(x, t) + c(x, t)) = 0, \quad (13)$$

so that N is a constant.

C. Equivalent Langevin equation description

Here, we go beyond the mean-field approximation Eq. (10,11,12) and obtain the exact stochastic partial differential equations that govern the quasispecies dynamics. To do so, shift conjugate fields as follows $a^* = 1 + \tilde{a}$, $b^* = 1 + \tilde{b}$,

and $c^* = 1 + \tilde{c}$, then we can write the action as follows:

$$\begin{aligned} S = & \int dt d^d x [\tilde{a}(\partial_t a - D_s \nabla^2 a + A a b + A_e a c - r_b - r_e c) \\ & + \tilde{b}(\partial_t b - D_I \nabla^2 b - A Q a b + r_b) + \tilde{c}(\partial_t c - D_e \nabla^2 c - A(1 - Q) a b - A_e a c + r_e c) \\ & - A Q a b (\tilde{b}^2 - \tilde{a} \tilde{b}) - A(1 - Q) a b (\tilde{b} \tilde{c} - \tilde{a} \tilde{b}) - A_e a c (\tilde{c}^2 - \tilde{a} \tilde{c})]. \end{aligned} \quad (14)$$

The next step is to introduce Gaussian-distributed noise fields $\eta_a(x, t), \eta_b(x, t), \eta_c(x, t)$ which will permit us to integrate over the conjugate fields and obtain the exact and *equivalent Langevin representation* of the stochastic dynamics contained in S . Now the part in $-S$ quadratic in the conjugate fields $\tilde{a}, \tilde{b}, \tilde{c}$ contributes to the exponential weight the following expression (we suppress writing out the x, t dependence and the integrals $\int d^d x dt$; these are understood to be included in what follows):

$$\begin{aligned} \exp(-S)|_{\text{quadratic}} &= \exp\left(+A Q a b \tilde{b}^2 - A a b \tilde{a} \tilde{b} + A(1 - Q) a b \tilde{b} \tilde{c} + A_e a c (\tilde{c}^2 - \tilde{a} \tilde{c})\right) \\ &= \exp\left(+\mathbf{S} \cdot \mathbf{V} \cdot \mathbf{S}\right) \\ &= \exp \sum_{ij} S_i V_{ij} S_j, \end{aligned} \quad (15)$$

where the vector $\mathbf{S} = (\tilde{a}, \tilde{b}, \tilde{c})$ and the 3×3 array \mathbf{V} is given by

$$\begin{pmatrix} 0 & -\frac{1}{2} A a b & -\frac{1}{2} A_e a c \\ -\frac{1}{2} A a b & +A Q a b & +\frac{1}{2} A(1 - Q) a b \\ -\frac{1}{2} A_e a c & +\frac{1}{2} A(1 - Q) a b & +A_e a c \end{pmatrix}. \quad (16)$$

Now make use of the Hubbard-Stratanovich transformation:

$$\int \prod_i d\eta_i \exp \left\{ -\frac{1}{4} \sum_{ij} \eta_i (V_{ij}^{-1}) \eta_j + \sum_i \eta_i S_i \right\} = \text{constant} \times \exp \sum_{ij} S_i V_{ij} S_j, \quad (17)$$

to express the righthand side of Eq. (15) as an integral over noise fields (η_i) . The covariance matrix \mathbf{V} is actually a 3×3 matrix in field space and is proportional to space and time delta functions (infinite dimensional continuous “matrices”, etc.) We immediately read off the direct and crossed noise correlations directly from V_{ij} , since

$$\mathbf{V} = \begin{pmatrix} \langle \eta_a \eta_a \rangle & \langle \eta_a \eta_b \rangle & \langle \eta_a \eta_c \rangle \\ \langle \eta_b \eta_a \rangle & \langle \eta_b \eta_b \rangle & \langle \eta_b \eta_c \rangle \\ \langle \eta_c \eta_a \rangle & \langle \eta_c \eta_b \rangle & \langle \eta_c \eta_c \rangle \end{pmatrix}. \quad (18)$$

For the final step we use Eq. (17) to replace the right hand side of Eq. (15) in Eq. (14). We can now integrate exactly over the conjugate fields $\tilde{a}, \tilde{b}, \tilde{c}$, appearing in the path integral $\int \mathcal{D}a \mathcal{D}\tilde{a} \mathcal{D}b \mathcal{D}\tilde{b} \mathcal{D}c \mathcal{D}\tilde{c} e^{-S[a, \tilde{a}, b, \tilde{b}, c, \tilde{c}]}$ which yields a product of delta-functional constraints which imply the following set of exact coupled set of Langevin equations:

$$\partial_t a = D_s \nabla^2 a - A a b - A_e a c + r_b + r_e c + \eta_a, \quad (19)$$

$$\partial_t b = D_I \nabla^2 b + A Q a b - r_b + \eta_b, \quad (20)$$

$$\partial_t c = D_e \nabla^2 c + A(1 - Q) a b + A_e a c - r_e c + \eta_c, \quad (21)$$

with noise correlations (compare (16) with (18))

$$\langle \eta_a(x, t) \rangle = \langle \eta_b(x, t) \rangle = \langle \eta_c(x, t) \rangle = 0 \quad (22)$$

$$\langle \eta_a(x, t) \eta_a(x', t') \rangle = 0 \quad (23)$$

$$\langle \eta_b(x, t) \eta_b(x', t') \rangle = +A Q a(x, t) b(x, t) \delta^d(x - x') \delta(t - t') \quad (24)$$

$$\langle \eta_c(x, t) \eta_c(x', t') \rangle = +A_e a(x, t) c(x, t) \delta^d(x - x') \delta(t - t') \quad (25)$$

$$\langle \eta_a(x, t) \eta_b(x', t') \rangle = -\frac{1}{2} A a(x, t) b(x, t) \delta^d(x - x') \delta(t - t') \quad (26)$$

$$\langle \eta_a(x, t) \eta_c(x', t') \rangle = -\frac{1}{2} A_e a(x, t) c(x, t) \delta^d(x - x') \delta(t - t') \quad (27)$$

$$\langle \eta_b(x, t) \eta_c(x', t') \rangle = +\frac{1}{2} A(1 - Q) a(x, t) b(x, t) \delta^d(x - x') \delta(t - t'). \quad (28)$$

Note the noise η_a has finite cross correlations Eqs.(26,27) but zero autocorrelation Eq.(23). This is already a indicator that the noise cannot be purely real. In the following Section, we will show that the pattern of the above correlations is solved by complex noise.

III. LANGEVIN EQUATIONS WITH COMPLEX NOISE

It is reasonable to assume that both the replicating and mutant species diffuse with equal rates $D_{Te} = D_I = D$ and have equal degradation rates, i.e. $r_e/r = 1$. We thus consider the following reaction-diffusion system, in a two-dimensional space, subject to noise and employing the *dimensionless* fields, noises and model parameters (for the details of the non-dimensionalization of the stochastic reaction-diffusion system, see Appendix A):

$$\begin{aligned}\frac{\partial \bar{a}}{\partial \tau} &= (D_s/D)\hat{\nabla}^2 \bar{a} - \bar{a}\bar{b} - \bar{a}\bar{c} + \bar{b} + \frac{1}{\delta}\bar{c} + \hat{\eta}_a \\ \frac{\partial \bar{b}}{\partial \tau} &= \hat{\nabla}^2 \bar{b} + Q\bar{a}\bar{b} - \bar{b} + \hat{\eta}_b \\ \frac{\partial \bar{c}}{\partial \tau} &= \hat{\nabla}^2 \bar{c} + \delta(1-Q)\bar{a}\bar{b} + \delta\bar{a}\bar{c} - \bar{c} + \hat{\eta}_c,\end{aligned}\quad (29)$$

where $\hat{\nabla}^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}$ and $\vec{\eta} = (\hat{\eta}_b, \hat{\eta}_c, \hat{\eta}_a)$ is the noise vector defined above. The initial condition $\bar{a}_0, \bar{b}_0, \bar{c}_0$ and the ratio of replication rates $\delta = \frac{A_e}{A} < 1$ obeys the dimensionless constraint for the closed system $\bar{N} = \int \int d\hat{x} d\hat{y} (\bar{a}_0 + \bar{b}_0 + \frac{\bar{c}_0}{\delta})$. In the two-dimensional case the total number of particles is given by the ratio $N = \bar{N}/\epsilon$ where $\epsilon = A/D_I$ is the ratio of the reaction to the diffusion processes (in any dimension d , we have $\epsilon = (r/D_I)^{d/2} A/r$).

In the deterministic case and per each single cell $\delta\hat{x} \times \delta\hat{y}$, this reaction-diffusion system Eq. (29) has the following set of homogeneous and static solutions:

- $\bar{b} = \bar{c} = 0, \bar{a} = \bar{N}$, absorbing solution
- $\bar{b} = 0, \bar{c}/\delta = \bar{N} - \frac{1}{\delta}, \bar{a} = \frac{1}{\delta}$, if $\delta > 1/\bar{N}$
- $\bar{c}/\delta = \frac{(\bar{N}Q-1)(1-Q)}{Q(1-\delta)}, \bar{b} = \frac{(\bar{N}Q-1)(Q-\delta)}{Q(1-\delta)}, \bar{a} = 1/Q$ if $Q > \delta$ and $Q > 1/\bar{N}$.

For convenience we can reorder the noise vector components $\vec{\eta} = (\hat{\eta}_b, \hat{\eta}_c, \hat{\eta}_a)$ such that it has the correlation matrix:

$$B = \langle \vec{\eta} \vec{\eta}^T \rangle = \begin{pmatrix} \epsilon Q \bar{a} \bar{b} & \frac{1}{2} \epsilon \delta (1-Q) \bar{a} \bar{b} & -\frac{1}{2} \epsilon \bar{a} \bar{b} \\ \frac{1}{2} \epsilon \delta (1-Q) \bar{a} \bar{b} & \epsilon \delta^2 \bar{a} \bar{c} & -\frac{1}{2} \epsilon \delta \bar{a} \bar{c} \\ -\frac{1}{2} \epsilon \bar{a} \bar{b} & -\frac{1}{2} \epsilon \delta \bar{a} \bar{c} & 0 \end{pmatrix}, \quad (30)$$

where the zero autocorrelation term is located in the last column and last row. Notice that B is a symmetric matrix with $\det B = -\frac{Q}{4} \bar{a}^3 \bar{b} \bar{c} \epsilon^3 \delta^2 (\bar{b} + \bar{c})$, i.e. it is negative definite.

For an $M \times M$ symmetric matrix B , one can apply the Cholesky decomposition $B = LL^T$ to extract the square root of the matrix in the form of a lower triangular matrix L with $L_{ii} = \sqrt{B_{ii} - \sum_{k=1}^{i-1} L_{ik}^2}$ and $L_{ji} = \frac{1}{L_{ii}}(B_{ji} - \sum_{k=1}^{i-1} L_{ik} L_{jk})$ and $j = i+1, \dots, M$. This decomposition is used when the symmetric matrix is positive definite. We have applied this algorithm to our case with negative definite correlation matrix and we obtain then the matrix “square root” L where some of the terms are manifestly imaginary:

$$L = \sqrt{\epsilon \bar{a}} \begin{pmatrix} \sqrt{Q} \bar{b} & 0 & 0 \\ \frac{\delta}{2}(1-Q)\sqrt{b/Q} & \frac{\delta\sqrt{4Q\bar{c}-(1-Q)^2\bar{b}}}{2\sqrt{Q}} & 0 \\ -\frac{1}{2}\sqrt{b/Q} & \frac{1}{2\sqrt{Q}} \frac{(1-Q)\bar{b}-2Q\bar{c}}{\sqrt{4Q\bar{c}-(1-Q)^2\bar{b}}} & \sqrt{-1}\sqrt{Q} \frac{\sqrt{\bar{b}\bar{c}+\bar{c}^2}}{\sqrt{4Q\bar{c}-(1-Q)^2\bar{b}}} \end{pmatrix}. \quad (31)$$

We will use this decomposition to relate the noise to a new *real* noise $\vec{\xi}$, a white Gaussian noise with $\langle \vec{\xi} \vec{\xi}^T \rangle = 1$ (i.e. with uncorrelated real components) such that $\vec{\eta} = L \vec{\xi}$ (and thus $\vec{\eta}^T = \vec{\xi}^T L^T$). We thus are able to write the internal noise as a linear combination of white noise terms. Notice that by doing so the condition $\langle \vec{\eta} \vec{\eta}^T \rangle = \langle L \vec{\xi} \vec{\xi}^T L^T \rangle = L \langle \vec{\xi} \vec{\xi}^T \rangle L^T = LL^T = B$ is satisfied. This transformation will allow us to separate the real and imaginary parts of the noise, a useful feature to have for setting up a numerical simulation of the system in Eq. (29).

Given three uncorrelated (real) white Gaussian noises ξ_1, ξ_2 and ξ_3 (the three components of $\vec{\xi}$) we recover $\hat{\eta}_b, \hat{\eta}_c$ and $\hat{\eta}_a$ with the specified cross-correlations Eqs. (A11-A16) by writing:

$$\begin{aligned}\hat{\eta}_b &= \sqrt{\epsilon \bar{a}} \sqrt{Q} \bar{b} \xi_1 \\ \hat{\eta}_c &= \sqrt{\epsilon \bar{a}} \left(\frac{\delta}{2}(1-Q)\sqrt{b/Q} \xi_1 + \frac{\delta\sqrt{4Q\bar{c}-(1-Q)^2\bar{b}}}{2\sqrt{Q}} \xi_2 \right) \\ \hat{\eta}_a &= \sqrt{\epsilon \bar{a}} \left(-\frac{\sqrt{b}}{2\sqrt{Q}} \xi_1 + \frac{1}{2\sqrt{Q}} \frac{(1-Q)\bar{b}-2Q\bar{c}}{\sqrt{4Q\bar{c}-(1-Q)^2\bar{b}}} \xi_2 + \sqrt{-1}\sqrt{Q} \frac{\sqrt{\bar{b}\bar{c}+\bar{c}^2}}{\sqrt{4Q\bar{c}-(1-Q)^2\bar{b}}} \xi_3 \right).\end{aligned}\quad (32)$$

The noise $\hat{\eta}_a$ for the nutrient field *always* has an imaginary component and, since this noise is *feeding* the nutrient field reaction-diffusion equation, the nutrient field also has an imaginary component. Finally since all the equations are coupled to the nutrient \bar{a} , even if the initial condition for $\bar{a}, \bar{b}, \bar{c}$ is real, the fields will, in principle, have both real and imaginary part and thus we have to solve a system of six partial differential equations, one for each field ($\text{Re}(\bar{a}), \text{Im}(\bar{a}), \text{Re}(\bar{b}), \text{Im}(\bar{b}), \text{Re}(\bar{c}), \text{Im}(\bar{c})$) with two-dimensional diffusion and noise. At this juncture, it is important that we confirm numerically that the complex solutions, once averaged over the fluctuations, do indeed yield real results, in accord with the theoretical expectations [17].

IV. NUMERICAL RESULTS

By inspection of the correlation matrix (30) we see that the internal, unavoidable, reaction noise is multiplicative and its intensity is proportional to ϵ . The parameter ϵ is the ratio of the reaction to the diffusion processes (in $d = 2$, $\epsilon = A/D_I$ and $\epsilon\delta = A_e/D_e$). The multiplicative noise is proportional both to \bar{a} , and either \bar{b} or a combination of \bar{b} with \bar{c} . If the system stays close to the mean field result, then $\bar{a} = 1/Q$ and \bar{b} and \bar{c} scale as $(\bar{N}Q - 1)$. Finally, the multiplicative noise will increase with both increasing ϵ and/or increasing \bar{N} . Only when the diffusion processes dominate and $\epsilon \rightarrow 0$, does the noise terms vanish, the local details of reaction are erased, and we expect to recover the homogeneous solution of the mean-field approximation. Our main interest here is the limit when the diffusion does not dominate, $\epsilon > 0$ and the noisy multiplicative term has a significant contribution. In this regime the problem can thus not be analyzed by perturbation theory and has to be treated numerically.

The numerical simulations of system evolution have been performed using forward Euler integration of the finite-difference equations following discretization of space and time in the stochastic partial differential equations. The spatial mesh consists of a lattice of 154×154 cells with cell size $\Delta\hat{x} = \Delta\hat{y} = 0.35$ and periodic boundary conditions. Noise has been discretized as well. The system has been numerically integrated up to $\tau = 100$ (with time step $\Delta\tau = 2.5 \times 10^{-4}$). Integrating the system numerically we confirmed that the imaginary fields were zero in average as expected, since the stochastic averages $\langle a \rangle, \langle b \rangle$, and $\langle c \rangle$ correspond to the physical densities and thus the scaled number of particles was preserved and remained *real*: $\text{Re}(\bar{N}) = \bar{N}$, and $\text{Im}(\bar{N}) = 0$ (within computational errors) [20].

This method is able to provide the time evolution of the spatial distribution of each of the fields. As an example we consider the evolution of the spatially uniform initial condition, $\bar{a} = 1/Q, \bar{b} = \frac{(\bar{N}Q-1)(Q-\delta)}{Q(1-\delta)}, \bar{c}/\delta = \frac{(\bar{N}Q-1)(1-Q)}{Q(1-\delta)}$ (which is the solution of mean-field problem) for $D_s/D = 10$, $Q = 0.92$, $\delta = 0.8$ and $\bar{N} = 100$ and noise intensity $\epsilon = 1$. In Fig. 1 we show the time evolution of the real part of the distributions of the master (\bar{b}) and mutant (\bar{c}) species, which exhibit spatial fluctuations with respect to the mean-field value (up to $\pm 1\%$ in black and $\pm 1\%$ in white). The spatial distributions of the master and mutant species are anti-correlated. After a transient time, the short-range spatial fluctuations (e.g., at $\tau = 0.5$) evolve into long-range spatial fluctuations (e.g., at $\tau = 75$) with wider regions of higher densities of either one or the other species. The system converges always to the same *spatially averaged* solution independently of the initial condition and noise intensity. For example, in Fig. 2-(Left) we show for $D_s/D = 10$, $Q = 0.92$, $\delta = 0.8$ and $\bar{N} = 100$, the time evolution of the *spatially averaged* solution ($\langle \bar{a}(\tau) \rangle = \int \int d\hat{x} d\hat{y} \bar{a}(\hat{x}, \hat{y}, \tau)$, etc.) for two noise intensities, $\epsilon = 0.1$ and $\epsilon = 10^{-2}$, when the initial condition is set to $\bar{a}(\hat{x}, \hat{y}, 0) = \bar{b}(\hat{x}, \hat{y}, 0) = \bar{c}(\hat{x}, \hat{y}, 0)/\delta = \bar{N}/3$. We can see that independently of the noise intensity this averaged value converges to the solution of the mean-field problem $\bar{a} = 1/Q, \bar{b} = \frac{(\bar{N}Q-1)(Q-\delta)}{Q(1-\delta)}, \bar{c}/\delta = \frac{(\bar{N}Q-1)(1-Q)}{Q(1-\delta)}$. Higher order moments, such as the mean square value, can be also extracted from the distribution. For the same study case we show the time evolution of the mean square value ($\sigma_{\bar{b}(\tau)} = \sqrt{\langle (\bar{b}(\tau) - \langle \bar{b}(\tau) \rangle)^2 \rangle}$) for three noise intensities, $\epsilon = 1, \epsilon = 0.1$ and $\epsilon = 0.01$, Fig. 2-(Right), confirming that only in the limit $\epsilon \rightarrow 0$ do spatio-temporal fluctuations vanish and we recover the homogeneous stationary solution of the mean-field approximation.

V. DISCUSSION

Starting from the microscopic kinetic equations for a single master species competing with mutants for a limited pool of nutrients, we have derived a set of stochastic partial differential equations that exactly describe the complete dynamics of this closed reacting and diffusing system. The unavoidable fluctuations inherent to the system give rise to multiplicative noise having both real and imaginary components. A procedure is presented to solve numerically this set of partial differential equations. The internal noise associated with the microscopic details of the reaction produces unavoidable spatio-temporal density fluctuations around the mean field value. We estimate the size of these fluctuations. They strictly vanish, and the mean-field limit is recovered, only when the diffusion processes are much faster than the rate of master species amplification. We find that the averages $\langle \bar{a} \rangle, \langle \bar{b} \rangle$ and $\langle \bar{c} \rangle$ tend to stationary values (see Fig 2-(Left)) as do also the second moments, or variances, $\sigma_{\bar{a}(\tau)}, \sigma_{\bar{b}(\tau)}$ and $\sigma_{\bar{c}(\tau)}$, see Fig 2-(Right).

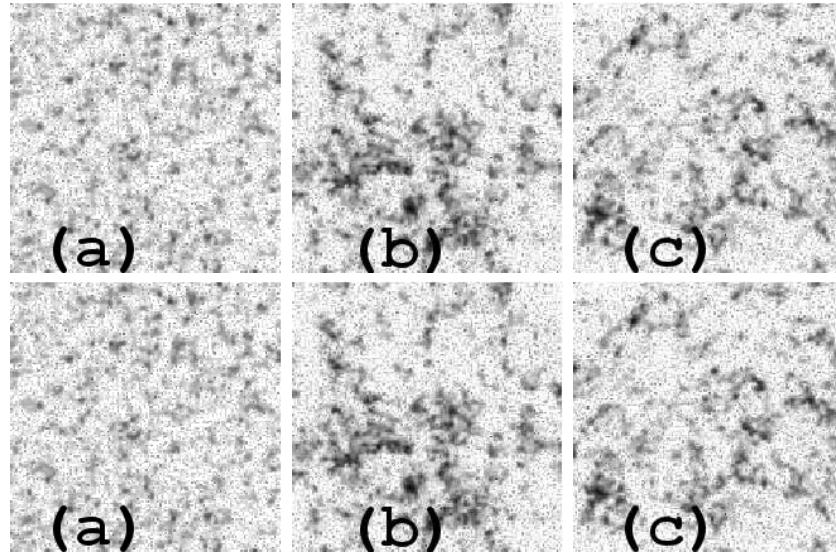


FIG. 1: Temporal sequence of spatial fluctuations in the real part of the stochastic fields $\bar{b}(\hat{x}, \hat{y}, \tau)$ (upper row) and $\bar{c}(\hat{x}, \hat{y}, \tau)$ (lower row). The spatial distributions are shown in (a) at $\tau = 0.5$, in (b) at $\tau = 50$ and in (c) at $\tau = 75$.

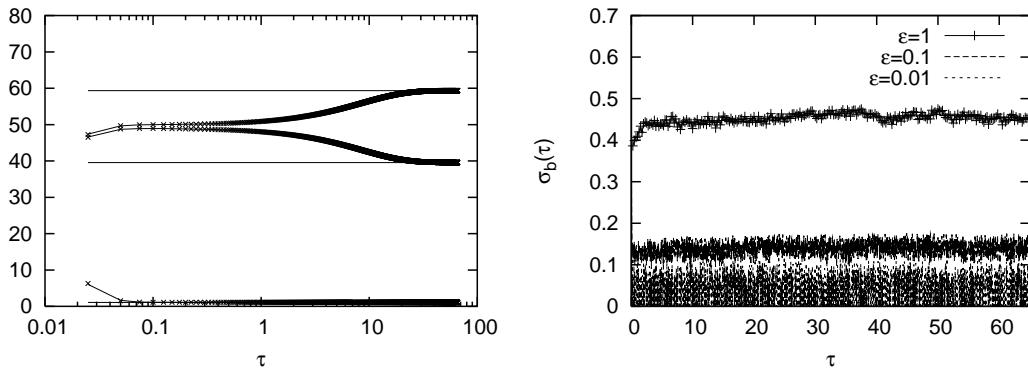


FIG. 2: (Left) Time evolution of spatially averaged values (upper curve for $\langle \bar{b} \rangle$, middle for $\langle \bar{c} \rangle / \delta$ and lower for $\langle \bar{a} \rangle$) for $\bar{N} = 100$, $\epsilon = 0.1$ and $\epsilon = 0.01$ (the difference in these two noise levels is not distinguishable in the figure) when the initial condition was set to $\bar{a}(\hat{x}, \hat{y}, 0) = \bar{b}(\hat{x}, \hat{y}, 0) = \bar{c}(\hat{x}, \hat{y}, 0) / \delta = \bar{N} / 3$. The *spatially averaged* solution always converges to the mean-field solution which is marked by the horizontal lines. (Right) Time evolution of the mean square value $\sigma_{\bar{b}(\tau)}$ for $\epsilon = 1$, $\epsilon = 0.1$ and $\epsilon = 0.01$ showing that the spatial fluctuations scale with the noise intensity, vanishing only in the limit $\epsilon \rightarrow 0$.

The general purpose algorithm presented here expresses a set of complex Gaussian noises with defined covariance matrix as a linear combination of real, white Gaussian noises. This allows for the numerical generation of this noise, and thus the numerical integration of Langevin-type equations with complex noise. We have performed numerical simulations with these dynamical equations to assess directly the influence of this noise on the evolution of the stochastic fields associated with a quasispecies, its error tail and the activated monomer distributions. Apart from the specific application to the problem analyzed in this paper, we believe this matrix decomposition will be of great practical use for simulating other stochastic PDEs with complex noise, a subject which has received little attention up to now [7]. In this regard it is interesting to emphasize that the appearance and necessity of complex and/or imaginary noise in probabilistic descriptions of both quantum optics and nonlinear chemical reaction systems has been recognized for some time now and began to be placed on a firm theoretical footing well over twenty years ago [18].

The simulations are carried out in $d = 2$ space dimensions. For this dimension, the basic amplitude of the noise is controlled by the dimensionless parameter $\epsilon = A/D_I$, where A denotes the amplification rate of the quasispecies and D_I its diffusion. Thus, the noise is controlled, in part, by the competition between production and diffusion.

Diffusion tends to erase or smooth out local concentration gradients while particle production, which occurs locally, tends to increase them (i.e., increases the local density of the species being amplified). In $d = 2$ and using Eq. (A1), we can also write $\epsilon = t_D/t_A$, where t_D, t_A denote the diffusion and species amplification time scales, respectively. This shows that the noise arises through the competition between these two time scales. Furthermore, since the noise is *multiplicative*, its amplitude also depends on the bilinear product of concentration fields (see, e.g., Eqs. (A10- A16)) so that whenever monomer and replicator or monomer and error tail meet at a point and react, this gives rise to noise at that point, whose strength is directly proportional to the product of particle concentrations at that point (equal to the product of particle numbers per unit area). Thus the complete noise amplitude is modulated by ϵ and the local bilinear concentrations. So, while diffusion smooths out inhomogeneities and tends to diminish the internal noise, increasing the total fixed particle number N (in a bounded domain) leads to stronger local fluctuations. This is easy to understand since, in spite of the diffusion, increasing N leads to a “pile-up” of reactants at spatial points. There will always be fluctuations about this approximate homogeneous state, and the statistical deviation from homogeneity grows with increasing total particle number.

In realistic situations with finite diffusion rates, the system does not converge to a homogeneous solution with a unique defined value, but to a state where the densities fluctuate both in space and time around a mean value. This approach is useful to estimate the expected deviations of the densities with respect to the mean-field value when the microscopic reaction details are taken into account. For systems with higher degree of non-linearity these deviations may eventually lead the system to new asymptotic states and also induce the formation of true patterns. We point out that no true spatial patterns are generated by the underlying reaction diffusion model studied in this paper. The model as it stands is weakly non-linear, depending only quadratically on the fields and these second-order reaction terms are not capable of giving rise to spatial patterns. The proper inclusion of noise induces random structures. However, once catalyzed self-replication is included, thereby leading to a bona-fide *network* of quasispecies, the underlying dynamics becomes cubically nonlinear, and cubic terms can lead to a variety of possible spatial patterns [13] whose evolution and stability properties in presence of internal noise can be profitably studied with the methods offered in this paper [15]. Finally, we mention that the methods in [3],[4] were used recently to study the critical behavior of a simple model of quasispecies in the vicinity of the error-threshold [19].

Acknowledgments

We thank Carlos Escudero for useful discussions and for independently working out some preliminary analytic calculations inspired by our model. M.-P.Z. is supported by a fellowship provided by INTA for training in astrobiology. The research of D.H. is supported in part by funds from CSIC and INTA and F.M. is supported in part by grant BMC2003-06957 from MEC (Spain).

APPENDIX A: NONDIMENSIONALIZATION

For the purposes of numerical simulation, it is convenient to cast the system of stochastic partial differential equations Eqs. (19-21) and noise statistics Eqs. (22-28) in terms of dimensionless fields and parameters. To this end, define basic length and time scales L and T , respectively. Then dimensional analysis of any of the three stochastic equations in Eqs. (19-21) yields

$$[a] = [b] = [c] = L^{-d}, \quad [D_I] = [D_e] = [D_s] = L^2/T \quad [Q] = 1, \quad [A] = [A_e] = L^d/T, \quad (\text{A1})$$

$$[r] = [r_e] = T^{-1}, \quad [\eta_a] = [\eta_b] = [\eta_c] = T^{-1}L^{-d}. \quad (\text{A2})$$

Define the dimensionless fields:

$$\bar{a} = \frac{A}{r}a, \quad \bar{b} = \frac{A}{r}b, \quad \bar{c} = \frac{A_e}{r}c, \quad (\text{A3})$$

and the dimensionless time and spatial coordinates and their corresponding derivative operators:

$$\tau = rt, \quad \hat{x}_j = \left(\frac{r}{D_I}\right)^{1/2} x_j, \quad (\text{A4})$$

$$\Rightarrow \quad \frac{\partial}{\partial \tau} = \frac{1}{r} \frac{\partial}{\partial t}, \quad \hat{\nabla}^2 = \left(\frac{D_I}{r}\right) \nabla^2. \quad (\text{A5})$$

We obtain the following dimensionless version of the stochastic equations listed in Eqs. (19-21):

$$\partial_\tau \bar{a} = \left(\frac{D_s}{D_I}\right) \hat{\nabla}^2 \bar{a} - \bar{a} \bar{b} - \bar{a} \bar{c} + \bar{b} + \left(\frac{r_e A}{r A_e}\right) \bar{c} + \hat{\eta}_a, \quad (\text{A6})$$

$$\partial_\tau \bar{b} = \hat{\nabla}^2 \bar{b} + Q \bar{a} \bar{b} - \bar{b} + \hat{\eta}_b, \quad (\text{A7})$$

$$\partial_\tau \bar{c} = \left(\frac{D_e}{D_I}\right) \hat{\nabla}^2 \bar{c} + \frac{A_e}{A} (1 - Q) \bar{a} \bar{b} + \frac{A_e}{A} \bar{a} \bar{c} - \frac{r_e}{r} \bar{c} + \hat{\eta}_c, \quad (\text{A8})$$

where the dimensionless noises are defined by

$$\hat{\eta}_a = \frac{A}{r^2} \eta_a, \quad \hat{\eta}_b = \frac{A}{r^2} \eta_b, \quad \hat{\eta}_c = \frac{A_e}{r^2} \eta_c, \quad (\text{A9})$$

and the dimensionless noise correlations are

$$\langle \hat{\eta}_a(\hat{x}, \tau) \rangle = \langle \hat{\eta}_b(\hat{x}, \tau) \rangle = \langle \hat{\eta}_c(\hat{x}, \tau) \rangle = 0 \quad (\text{A10})$$

$$\langle \hat{\eta}_a(\hat{x}, \tau) \hat{\eta}_a(\hat{x}', \tau') \rangle = 0 \quad (\text{A11})$$

$$\langle \hat{\eta}_b(\hat{x}, \tau) \hat{\eta}_b(\hat{x}', \tau') \rangle = +\epsilon Q \bar{a}(\hat{x}, \tau) \bar{b}(\hat{x}, \tau) \delta^d(\hat{x} - \hat{x}') \delta(\tau - \tau') \quad (\text{A12})$$

$$\langle \hat{\eta}_c(\hat{x}, \tau) \hat{\eta}_c(\hat{x}', \tau') \rangle = +\epsilon \delta^2 \bar{a}(\hat{x}, \tau) \bar{c}(\hat{x}, \tau) \delta^d(\hat{x} - \hat{x}') \delta(\tau - \tau') \quad (\text{A13})$$

$$\langle \hat{\eta}_a(\hat{x}, \tau) \hat{\eta}_b(\hat{x}', \tau') \rangle = -\frac{1}{2} \epsilon \bar{a}(\hat{x}, \tau) \bar{b}(\hat{x}, \tau) \delta^d(\hat{x} - \hat{x}') \delta(\tau - \tau') \quad (\text{A14})$$

$$\langle \hat{\eta}_a(\hat{x}, \tau) \hat{\eta}_c(\hat{x}', \tau') \rangle = -\frac{1}{2} \epsilon \bar{a}(\hat{x}, \tau) \bar{c}(\hat{x}, \tau) \delta^d(\hat{x} - \hat{x}') \delta(\tau - \tau') \quad (\text{A15})$$

$$\langle \hat{\eta}_b(\hat{x}, \tau) \hat{\eta}_c(\hat{x}', \tau') \rangle = +\frac{1}{2} \epsilon \delta(1 - Q) \bar{a}(\hat{x}, \tau) \bar{b}(\hat{x}, \tau) \delta^d(\hat{x} - \hat{x}') \delta(\tau - \tau'). \quad (\text{A16})$$

In arriving at this, note that

$$[\delta^d(x)] = L^{-d}, \quad [\delta(t)] = T^{-1}, \quad (\text{A17})$$

whereas the following deltas are dimensionless:

$$[\delta^d(\hat{x})] = 1, \quad [\delta(\tau)] = 1, \quad (\text{A18})$$

and

$$\delta^d(x) \delta(t) = r \left(\frac{r}{D_I}\right)^{d/2} \delta^d(\hat{x}) \delta(\tau). \quad (\text{A19})$$

The basic control parameters are given by

$$\epsilon = \frac{A}{r} \left(\frac{r}{D_I}\right)^{d/2}, \quad \delta = \left(\frac{A_e}{A}\right) < 1, \quad 1 \geq Q \geq 0. \quad (\text{A20})$$

Note that in $d = 2$ space dimensions the noise amplitude ϵ is determined uniquely by the ratio of the replication rate A to replicator diffusion D_I . It is reasonable to assume that both master sequence and error tail replicator molecules decay with the same rate, $r = r_e$. Moreover, since both the master sequence and error tail are built up from the same monomer pool and have the same total length, they should also have identical diffusion constants $D_I = D_e$. The much smaller monomers should diffuse more rapidly, so we can take $D_s \gg D_I = D_e \equiv D$. Lastly, we note that the noise-averaged fields satisfy the constraint:

$$\int d^2 \hat{x} \langle \bar{a} + \bar{b} + \frac{1}{\delta} \bar{c} \rangle = \bar{N} = \epsilon N, \quad (\text{A21})$$

where N is the total particle number.

The complete nondimensional model has five parameters: $\epsilon, \delta, Q, D_s/D > 1$ and \bar{N} .

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